REMARKS

Reconsideration of this application is requested in view of the amendments to the claims and the remarks presented herein.

The claims in the application are claims 24, 25, 27 to 30 and 32 to 35, all other claims having been cancelled. Claim 34 has been rewritten per the interview discussions.

Applicants wish to thank the Examiner in charge of the above application and Jose Dees, his SPE for the courtesies extended to the undersigned and J.F. Burtin, the French attorney for the Assignee and Dr. J. Paris and Dr. S. Delpy at the interview on November 14, 2001 when this application and related application Serial No. 423,109 filed on June 12, 2000 were discussed.

All of the claims were rejected over the Fraser et al reference and the Lanquetin et al patent for reasons of record. The Examiner was of the opinion that the Lanquetin et al patent taught a method of treating estrogen deficiencies which embraces Applicants' claimed method. With respect to the Fraser et al patent, the Examiner stated that Fraser et al taught estradiol in combination with a protestative compound for the treatment of estrogenic deficiencies which embraced Applicants' claimed invention.

Applicants respectfully traverse these grounds of rejection since the references in no way relate to the invention as presently claimed. Claim 34 now calls for treating functional disorders caused by hypoestrogenism in women and avoiding the appearance of osteoporosis, withdrawal bleeding and cardiovascular diseases in post-menopausal women by continuously without interruption orally administering to said women a combination of 0.5 to 3 mg of an estrogenic compound and 1.5 to 3.75 mg of nomegestrol acetate.

As pointed out at the interview, the Lanquetin et al patent teaches a sequential treatment first with estradiol, then with a estradiol and a progesterone and then, with a placebo. Fraser et al deals with a similar sequential treatment wherein the estradiol is a result of a subcutaneous implant but it is still a sequential treatment wherein the progesterone is only administered for a short period of time and followed by a break therein. Both of these trisequential treatments result in menstrual bleeding in accordance with a women's normal cycle.

In contrast thereto, Applicants' method comprises continuously without interruption administering both estradiol and the specific progesterone simultaneously with no interruption in the administration and this results in no bleeding. This can be seen from the table illustrating the different cycles as well as the table showing the differences between the three methods of administration. As can be seen from the latter treatment, both the

references use a sequential treatment whereas Applicants use a continuous treatment. The menstrual cycle in the two prior art references is regular but in Applicants' process, there is absolutely no menstrual cycle. There is withdrawal bleeding in both of the prior art references and no bleeding whatsoever in Applicants' method. Moreover, the endometrium is secretory in both instances in the prior art while Applicants' endometrium is atrophic. Applicants are submitting herewith both tables in color for the Examiner's convenience.

Applicants are submitting herewith a declaration by Dr. Sitruk-Ware Regine who has been a medical doctor since 1975 and is an outstanding expert in the field of endocrinology and is now a professor at Rockefeller University in New York. This declaration summarizes the fact that a progestin is needed to inhibit the effects of estrogen on the endometrium. The declaration also addresses the fact that the sequential and the continuous combined treatments have different effects on the endometrium and it goes on to further discuss the sequential and continuous and combined treatments having different effects on the breast. The declaration further demonstrates that different progestins do not have the same effects on the cardiovascular system. Therefore, it is deemed that the present record now overcomes the two rejections in view of the amendment to method claim 34.

At the interview, Applicants discussed the reissue patent No.

36,247 of Plunkett et al, a copy of which is submitted herewith for the Examiner's convenience. This patent does relate to continuous and uninterrupted administration of a progestogen and estrogen in daily doses. However, the progestins disclosed by the reference are entirely different and unrelated to Applicants' nomegestrol acetate. Applicants' progestin is distinct in the fact that it has no androgenic activity, no estrogenic activity, a high antimitotic activity and a perfect metabolic tolerance as compared to the progestins taught by Plunkett et al. The declaration of Dr. Sitruk-Ware demonstrates that different progestins do not have the same effect on the cardiovascular system.

Applicants are submitting herewith a table which profiles the nomegestrol acetate used by Applicants' process with the type of progestins taught by the Plunkett et al patent. It can be seen that Applicants' nomegestrol has a strong progestative activity without androgenic effect which is contrary to the 19-nor testosterones and the MPA taught in Plunkett et al. Applicants' compound also is without any estrogenic effect which is contrary to the 19-nor testosterones and has a strong anti-estrogenic effect in contrast to the MPA of Plunkett et al.

Applicants' product further has a strong anti-antimitotic effect which is contrary to the MPA. Applicants' compound further has a strong anti-gonadotropic effect which again, is contrary to the MPA and a perfect metabolic tolerance which is contrary to 19-

testosterone and MPA. Moreover, with Applicants' composition, there is no deleterious effect on blood vessels which again, is contrary to the MPA. Therefore, it is clearly established that Applicants' progestin is entirely different from those disclosed in the prior art. Therefore, the Plunkett et al reference does not anticipate or render obvious Applicants' invention and a rejection based thereon is not proper.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Bierman, Muserlian and Lucas

By: 

Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

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Enclosures